

CLAIMS

1. A method of infecting the glomerular cells of a kidney of a mammalian subject
5 requiring same with a recombinant adenovirus vector carrying a gene or genes of interest,
comprising the step of infusing intra-renal arterially in a single pass through the superior
mesenteric artery or renal artery an effective amount of said adenoviral vector into said
kidney at an effectively slow rate over an effective period of time, under conditions such
that at least 30% of said glomerular cells are infected with said vector.

10 2. The method according to claim 1, wherein said adenovirus vector carries a control
element that preferentially expresses said gene or genes into renal glomerular cells.

15 3. The method according to claim 1, wherein said kidney is maintained at reduced
temperatures during said infusion procedure,

20 4. The method according to claim 1, further comprising clamping the aorta above and
below said superior mesenteric renal artery of said kidney, and infusing through said
superior mesenteric renal artery.

5. The method of claim 1, wherein said renal artery is cannulated directly without
clamping of said aorta during said infusion.

25 6. The method of claim 1, wherein said mammal is a rodent, said rate of infusion is
about $0.1 - 0.5 \times 10^{11}$ particles per minute, and said effective period of adenoviral vector
infusion is between about 15 and 120 minutes.

30 7. The method according to claim 1, further comprising concurrent cannulation of
the femoral vein through the vena cava into the renal vein so as to direct vector not taken
up by renal glomerular cells away from the general circulation.

Table 1. Adenovirus-mediated gene transfer to rat kidney

Animal No	Viral dose (particles/rat)	Perfusion time (min)	Sac'd at	Lac Z expression		
				right kidney	left kidney	liver
1-1	1.5 x 10 ¹¹	5	day 3 post infusion	0%	0%	10%
1-2				0%	0%	60%
1-3				0%	0%	30%
2-1	1.5 x 10 ¹¹	15	day 3 post infusion	0%	0%	70%
2-2				0%	0%	60%
2-3				0%	0%	40%
3-1	7.5 x 10 ¹¹	5	day 3 post infusion	0%	0%	95%
3-2				0%	0%	70%
3-3				0%	0%	80%
4-1	7.5 x 10 ¹¹	15	day 3 post infusion	30% glomeruli	0%	80%
4-2				50% glomeruli	0%	100%
4-3				70% glomeruli	0%	100%
5-1	7.5 x 10 ¹¹	15	day 21 post infusion	10% glomeruli	0%	30%
5-2				10% glomeruli	0%	50%
5-3				15% glomeruli	0%	40%

Tissue samples from four animals were examined at each time point. Quantification was made by counting lacZ positive cells (in liver) or renal glomeruli in ten microscopic fields with 100x magnification. A lacZ positive glomerulus is defined as a glomerulus that contains at least three lacZ positive cells.

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1-2				0%	0%	60%
1-3				0%	0%	30%
2-1	1.5 x 10 ¹¹	15	day 3 post infusion	0%	0%	70%
2-2				0%	0%	60%
2-3				0%	0%	40%
3-1	7.5 x 10 ¹¹	5	day 3 post infusion	0%	0%	95%
3-2				0%	0%	70%
3-3				0%	0%	80%
4-1	7.5 x 10 ¹¹	15	day 3 post infusion	30% glomeruli	0%	80%
4-2				50% glomeruli	0%	100%
4-3				70% glomeruli	0%	100%
5-1	7.5 x 10 ¹¹	15	day 21 post infusion	10% glomeruli	0%	30%
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